

What is claimed is:

1. A composition comprising a combination of ATP-depleting
5 agents at concentrations which deplete the ATP level to
at least 15% of normal in cancer cells wherein at least
one of the ATP-depleting agents is a mitochondrial ATP-
inhibitor, a glycolytic inhibitor, a methylthioadenosine
phosphorylase inhibitor or an inhibitor of De Novo purine
10 synthesis other than 6-Methylmercaptapurine riboside.
2. A composition comprising an effective amount of a
combination of ATP-depleting agents at concentrations
which deplete the ATP level to at least 15% of normal in
15 cancer cells wherein at least one of the ATP-depleting
agents is a mitochondrial ATP-inhibitor, a glycolytic
inhibitor, a methylthioadenosine phosphorylase inhibitor
or an inhibitor of De Novo purine synthesis other than 6-
Methylmercaptapurine riboside.
- 20 3. The composition of claim 1 or 2, wherein said composition
produces a substantially better effect than a composition
without at least one of the following ATP-depleting
agents: a mitochondrial ATP-inhibitor, a glycolytic
25 inhibitor, a methylthioadenosine phosphorylase inhibitor
or an inhibitor of De Novo purine synthesis other than 6-
Methylmercaptapurine riboside.
4. The composition of claim 1, 2 or 3, further comprising a
30 pyrimidine-depleting agent or a pyrimidine antagonist.
5. The composition of claim 1, 2 or 3, further comprising an
anticancer agent.
- 35 6. The composition of claim 5, wherein the anticancer agent

to which the cancer is sensitive.

- 5 7. The composition of claim 5 or 6, wherein the anticancer agent is at approximately half of the maximum tolerated dose.
- 10 8. The composition of claim 1-7, wherein the ATP-depleting agents is 6-methylmercaptapurine riboside (MMPR), 6-Aminonicotinamide (6-AN), alanosine (AL) or a combination thereof.
- 15 9. The composition of claim 8, further comprising N-(phosphonacetyl)-L-aspartic acid (PALA).
- 20 10. The composition of claim 9, further comprising 3-bromopyruvic acid.
- 25 11. The composition of claim 1-10 wherein the ATP-depleting agents is 6-methylmercaptapurine riboside (MMPR), alanosine (AL) or a combination thereof.
- 30 12. The composition of claim 11, further comprising N-(phosphonacetyl)-L-aspartic acid (PALA).
- 35 13. The composition of claim 11, further comprising dehydroepiandrosterone (DHEA).
14. The composition of claim 11, further comprising oxythiamine (OT).
15. The composition of claim 11, further comprising dehydroepiandrosterone (DHEA) and oxythiamine (OT).
16. The composition of claim 11, further comprising 6-Aminonicotinamide (6-AN).

17. The composition of claims 1-16, further comprising a cytokine.
18. The composition of claim 17, wherein the cytokine is G-CSF.
19. A pharmaceutical composition comprising the composition of claim 1-18 and a pharmaceutically acceptable carrier.
20. A method for treating a cancer subject comprising administering to the subject a combination of ATP-depleting agents at concentrations which deplete the ATP level to at least 15% of normal in cancer cells wherein at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.
21. A method for treating a cancer subject comprising administering to the subject a combination of ATP-depleting agents at concentrations which deplete the ATP level to at least 15% of normal in cancer cells wherein at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside, wherein said composition produces a substantially better effect than a composition without at least one of the following ATP-depleting agents: a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.

22. The method of claim 20 or 21, further comprising a pyrimidine-depleting agent.
- 5 23. The method of claim 20 or 21, further comprising an anticancer agent.
24. The method of claim 23, wherein the cancer is clinically sensitive to the employed anti-cancer agent.
- 10 25. The method of claim 23 or 24, wherein the anticancer agent is at approximately half of the maximum tolerated dose.
- 15 26. A method for induction of cancer cell death comprising contacting said cancer cell with a combination of ATP-depleting agents at concentrations which deplete the ATP level to at least 15% of normal in cancer cells wherein at least one of the ATP-depleting agents is a
20 mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptipurine riboside.
- 25 27. A method for induction of cancer cell death comprising contacting said cancer cell with a combination of ATP-depleting agents at concentrations which deplete the ATP level to at least 15% of normal in cancer cells wherein at least one of the ATP-depleting agents is a
30 mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptipurine riboside, wherein said composition produces a substantially better effect than a composition

without at least one of the following ATP-depleting agents: a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor and an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.

28. The method of claim 26 or 27, further comprising a pyrimidine-depleting agent.

29. The method of claim 26 or 27, further comprising an anticancer agent.

30. The method of claim 29, wherein the cancer is clinically sensitive to the employed anticancer agent.

31. The method of claim 29 or 30, wherein the anticancer agent is at half of the maximum tolerated dose.

32. A method for treating a cancer subject, or for the induction of cancer cell death, comprising administering to the subject a combination of ATP-depleting agents, a pyrimidine antagonist, and anticancer agent to which the treated cancer is sensitive, at concentrations which together collectively deplete the ATP levels to at least 15% of normal in cancer cells wherein at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.

33. A method for treating a cancer subject, or for the induction of cancer cell death, comprising administering to the subject a combination of ATP-depleting agents, a pyrimidine antagonist, and anticancer agent to which the treated cancer is sensitive, at concentrations which

together collectively deplete the ATP levels to at least 15% of normal in cancer cells, wherein at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine ribosidewherein and said composition produces a substantially better effect than a composition without at least one of the following ATP-depleting agents: a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor and an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.

34. The method of claim 32 or 33, wherein the anticancer agent is half of the maximum tolerated dose.

35. The method of claim 20-34, wherein the ATP-depleting agent is 6-methylmercaptapurine riboside (MMPR), 6-Aminonicotinamide (6-AN), alanosine (AL) or a combination thereof.

36. The method of claim 35, further comprising N-(phosphonacetyl)-L-aspartic acid (PALA).

37. The method of claim 35, further comprising 3-bromopyruvic acid.

38. The method of claim 35 wherein the ATP-depleting is 6-methylmercaptapurine riboside (MMPR), alanosine (AL) or a combination thereof.

39. The method of claim 35 further comprising N-(phosphonacetyl)-L-aspartic acid (PALA).

40. The method of claim 35 further comprising dehydroepiandrosterone (DHEA).
- 5 41. The method of claim 35 further comprising oxythiamine (OT).
42. The method of claim 35 further comprising dehydroepiandrosterone (DHEA) and oxythiamine (OT).
- 10 43. The method of claim 35 further comprising 6-Aminonicotinamide (6-AN).
44. The method of claim 20-43 further comprising a cytokine.
- 15 45. The method of claim 44, wherein the cytokine is G-CSF.
46. A method for treating drug-resistant cancer cells comprising contacting the said cancer with a combination of ATP-depleting agents and an anticancer agent.
- 20 47. The method of claim 46, wherein the dose of said anticancer agent is at approximately half of the maximal tolerated dose.
- 25 48. The method of claim 46, wherein the ATP level is depleted to at least 15% of normal in cancer cells and at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.
- 30 49. The method of claim 46, wherein the ATP level is depleted to at least 15% of normal in cancer cells and at

least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside and said composition produces a substantially better effect than a composition without at least one of the ATP-depleting agents: a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor and an inhibitor of De Novo purine synthesis other than 6-Methylmercaptapurine riboside.

50. A method for induction of cancer cell death comprising contacting said cancer cell with an agent capable of inducing necrosis in cancer cells.

51. The method of claim 50, wherein the agent is an ATP-depleting agent.

52. The method of claim 50 further comprising a pyrimidine-depleting regimen.

53. The method of claim 50 further comprising an anticancer agent.